autoantigens, in an amount effective to suppress an autoimmune response associated with said autoimmune disease].

REMARKS

Reconsideration of this application is respectfully requested.

By the present amendment, it has been made clear that the claimed treatment for autoimmune disease proceeds by suppression of an ongoing abnormal autoimmunity which by definition is of benefit to the treated subject since it avoids tissue damage resulting from the abnormal immune response by suppression of said response. Moreover, the claims are now limited to autoantigens without specifying fragments.

As a result, the Examiner's remarks at Section 6 et. seq. of the Office Action are not applicable to the present claims. The present method is not a cure but a treatment directed to the suppression of autoimmune response. Any tissue destruction that can be averted or delayed as a result of such suppression is of benefit to the treated subject, and within the present claims. Thus, even if determinant spreading has occurred, there is no evidence that recognition of the original determinant by the immune system will have ceased. Accordingly, oral or enteral administration of the autoantigen will continue to suppress at least the autoimmune response targeted against the same antigen.

Moreover, in several studies, there has been no evidence of anyone or any animal subject getting worse from oral administration of antigen, or mounting an immune response against the administered antigen. Accordingly, the Examiner's concerns do not

seem to be justified in light of the present invention, in light of such other studies, and in light of the evidence that the present application describes. Unlike the prior art, the present inventors postulated (and produced evidence in the application) that feeding antigen would set in motion the oral tolerance mechanisms that are involved in developing tolerance to food antigens (elicitation of suppressor T cells). Since persons with autoimmune disease do not usually have abnormal immune responses to food, the present inventors reasoned that they would respond with tolerance to fed autoantigen.

Since the present method treats the symptoms of abnormal autoimmune response and not the underlying cause of the disease, the unknown etiology of autoimmune disease is not believed to be relevant. The abnormal autoimmune response has been documented in autoimmune disease, and the Examiner does not dispute this. Since the present inventors have shown that the same type of tolerizing response occurs when antigen is ingested regardless of the type of antigen, it follows that it will work for any other antigen.

Hence, many of the Examiner's concerns in Section 6 would be completely legitimate before the experiments of the present application, but not after, for the following reasons:

A number of the experiments detailed in the specification support this hypothesis: Example 2 shows that the oral regimen suppressed autoimmune-like response in EAE after immunization, i.e., after induction of the autoimmune-like response. This is contrary to the Examiner's supposition that the present regimen would be effective only in

prevention of disease. See also Tables II and III. Similarly, Example 6 which shows that both encephalitogenic determinants and nonencephalitogenic determinants are effective to suppress autoimmune-like response, supports the applicants' and not the Examiner's position regarding possible determinant spreading. Also, the adoptive transfer experiments (Ex. 10) and the demonstration that the cells mediating suppression are not CD4 cells (Ex. 11) support the applicants' position that the orally induced tolerance is due to a mechanism (active induction of suppressor T-cells) that is common to rodents and humans and to subjects suffering from autoimmune disease or not and that is similar to tolerance induction towards food antigens and therefore independent of the particular autoimmune disease.

Lastly, evidence that the present invention works as predicted (in response to Section 5 of the Office Action) includes, among others, the following US patents issued to the present inventors and to their co-workers: USP No. 5,869,054; 5,869,093; 5,858,968; 5,935,577; 5,961,454; 6,036,957; 6,039,947; 6,077,509.

In every instance, there has been abatement of the harmful autoimmune response.

Accordingly, withdrawal of the rejections is respectfully requested and allowance of the present claims respectfully solicited.

Respectfully submitted,

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